134031-84-8; **41** (isomer 1), 134031-78-0; **41** (isomer 2), 134031-85-9; (+)-**42**, 134031-79-1; (+)-**46**, 125136-27-8; **49**, 124764-75-6; (+)-**50**, 125315-19-7; **51**, 134031-80-4; **52**, 134031-81-5; **53**, 134031-82-6; **54**, 134031-83-7; **55**, 125315-20-0; **56**, 125315-21-1; **57**, 125409-70-3; **58** (isomer 1), 125409-69-0; **58** (isomer 2), 125315-22-2; **59**, 125315-24-4; **60**, 125315-23-3; (+)-**63**, 117182-82-8; (+)-**64**, 80243-67-0; **65**, 117182-79-3; **66**, 117182-80-6; **67**, 117182-86-2; (-)-**68**, 117182-81-7; (+)-**69**, 117182-84-0.

C-Glycosylanthraquinone Synthesis: Total Synthesis of Vineomycinone B2 Methyl Ester

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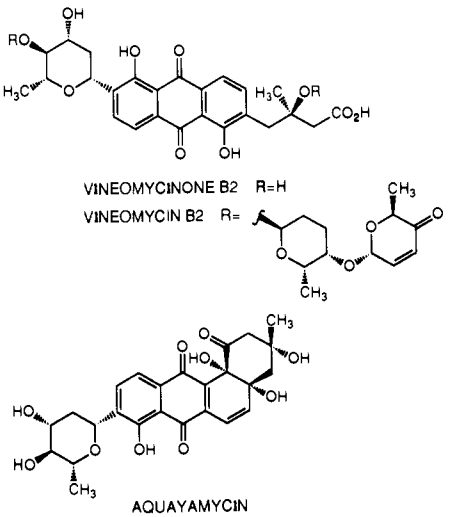
Abstract: A synthesis of substituted anthraquinones has been developed. Commercially available anthrarufin and 1,8-dihydroxyanthraquinone were converted to the corresponding (methoxymethoxy)anthracenes. Directed metalation followed by stannylation produced stable intermediates that were either alkylated, arylated, acylated, and/or C-glycosylated. The value of this new methodology was demonstrated by the triply convergent total synthesis of vineomycinone B2 methyl ester, a representative *C*-glycosylanthraquinone antibiotic.

Introduction

The clinical utility of the anthracyclines and their analogues in the chemotherapy of acute leukemia and solid tumors of the breast, lung, bladder, and ovary, as well as their interesting structures, has brought these compounds to the forefront of chemical synthesis.[3] Anthracyclines consist of an anthraquinone nucleus embedded within a hydrotetracene. Typically, one or more sugars are attached through *O*-glycosyl bonds. A fascinating class of structurally related compounds exists in which the anthraquinone portion of the molecule is linked to a carbohydrate through a C-glycosidic bond.[4] Two representatives of this class of compounds are vineomycin B2[5] and aquayamycin.[6] Aquayamycin is a powerful tyrosine hydroxylase and dopamine β-hydroxylase inhibitor.[6] The vineomycins are antitumor antibiotics that were first isolated from a culture of *Streptomyces matensis* subsp. *vineus*, which was active against Gram-positive bacteria and against sarcoma-180 solid tumors in mice.[5] Vineomycinone B2 methyl ester is derived from the acid-catalyzed methanolysis of vineomycin B2.

The characteristic structural features of vineomycinone B2 methyl ester (**1**) are the *C*-glycosyl bond to the olivose derivative and the alkyl side chain bearing a stereogenic center on the opposite end of the molecule. This combination of challenging structure and the interesting pharmacological properties has motivated efforts in organic synthesis. To date three groups in addition to our own have reported total syntheses of **1**.[7-9] Results



from our research have demonstrated the utility of a triply convergent approach to the synthesis of this structural type.[10,11] The experimental detail that was lacking in the preliminary communication,[11] as well as some new results, will be described.

Results and Discussion

The target molecule **1** was quite simple; therefore, it was felt that the retrosynthesis should also reflect this fact. The total synthesis that was devised was an opportunistic one, in the sense that it exploited the features peculiar to the molecule. The most obvious feature of **1** is the symmetry of the aromatic core, and it was felt that any successful synthesis would have to take advantage of this. Indeed, Danishefsky's inspired first total synthesis[7] made use of this feature and also demonstrated, unsurprisingly, that no transmission of stereochemical information took place

(1) Fellow of the Alfred P. Sloan Foundation, 1988-1991.
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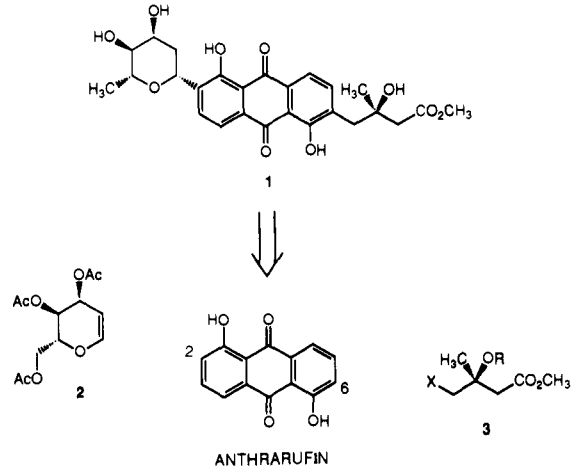
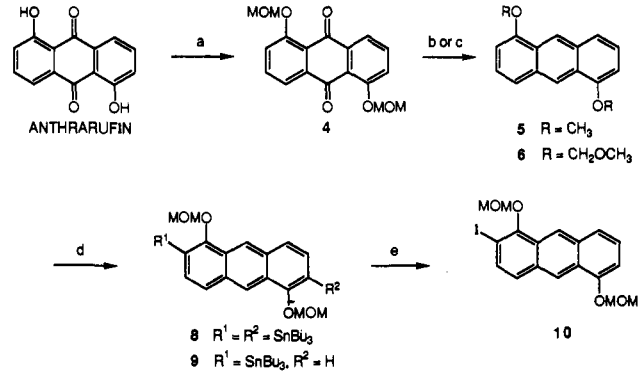
Scheme I



between the remote stereocenters on the two anthraquinone appendages. Our retrosynthesis, which is summarized in Scheme I, seemed an obvious one. Vineomycinone B2 can be easily perceived as arising from the conjunction of three subunits: an anthrarufin core linked to an olivose through a *C*-glycosyl bond at C2 and to a mevalonate side chain at C6. This analysis appeared reasonable, since both the anthrarufin and the olivose precursor, tri-*O*-acetyl-D-glucal (**2**), were cheap articles of commerce. Moreover, several synthetic equivalents to the chiral side chain **3** could be imagined. The problems of the total synthesis were to form the carbon–carbon bonds at C2 and C6, control the sugar *C*-glycosyl stereochemistry, and prepare an appropriate equivalent of **3**.

Because both substituents of **1** are ortho to the hydroxyl groups, their use to direct aromatic metalation suggested itself. The symmetry of anthrarufin induces a potential difficulty for the differential functionalization at C2 and at C6. Two solutions to this problem can be envisioned. Either different protecting/directing groups could be used for each of the two hydroxyls or both hydroxyls could be converted to the same derivative and conditions leading to sequential metalations could be developed. Both of these strategies were shown to be viable; however, the second approach was preferred for practical reasons. 1,5-Dihydroxyanthracene, the reduction product of anthrarufin, was not a practical starting material for this work. Dihydroxyanthracenes are extremely sensitive to air oxidation. Therefore, anthrarufin was converted to the bis(methoxymethyl) derivative **4** (Scheme II) in 73% yield by treatment with chloromethyl methyl ether and diisopropylethylamine in refluxing chloroform.[12] The methoxymethyl group appeared to be an apt choice because of its well-documented ability to direct metalation in aromatic and other systems.[13] The ortho-metalation of **4** failed under a variety of reaction conditions. This unsurprising result is presumably a consequence of unproductive metal ion chelation involving the carbonyl groups or competing electron transfer and addition of the alkyllithium to the quinone carbonyls.[14] A simple solution to this obstacle was to reduce anthraquinone **4** to anthracene **5**, since it was anticipated that reoxidation to the quinone at the end of the reaction sequence would be straightforward.[15] A variety of reagents have been suggested for the reduction of anthraquinones to anthracenes;[16] however, most methods rely upon a combination of a reducing

Scheme II[a]



[a] Key: (a) CH_3OCH_2Cl, *i*-Pr_2NEt, $CHCl_3$, reflux, 73%; (b) Et_3SiH, BF_3-Et_2O, 2 h, 65 °C, 15% of **5**; (c) $NaBH_4$ (excess), *i*-PrOH, reflux, 87% of **6**; (d) (i) *t*-BuLi, pentane, Et_2O, −10 °C, (ii) *n*-Bu_3SnCl, 74% of **9**; (e) I_2, CH_2Cl_2, 94%.

agent and a Lewis acid. Under these conditions the conversion of the methoxymethyl groups to *O*-methyls was a major reaction pathway. For example, treatment of **4** with triethylsilane and boron trifluoride etherate at 65 °C for 2 h produced 1,5-dimethoxyanthracene (**5**) in ca. 15% yield. Since the methoxyls were not effective directing groups for the metalation of **5**, alternative reduction conditions were developed. It is worth mentioning that a major difficulty encountered when working with anthracenes and anthraquinones is their low solubility in ethereal solvents. The failure of **5** to undergo effective ortho-metalation is due in part to its limited solubility, a problem common to many anthracenes. The successful reduction of **4** to **6** was accomplished with an excess of sodium borohydride in refluxing 2-propanol or ethanol in 87–90% yield. This method appears to be general and was applied to the preparation of anthracenes **5** (80–84% yield) and **7** (65–67% yield) from the corresponding anthraquinones. The mechanism of this reduction presumably requires fast reduction of both carbonyl groups followed by loss of water to form the anthrone as a transient intermediate. Rapid carbonyl reduction would be followed by aromatization through loss of a second water molecule.

The metalation at C2 of **6** was the next task. Treatment of **6** with 2.5 equiv of *tert*-butyllithium in ether at 25 °C for 2 h followed by quenching with 3.7 equiv of tributylchlorostannane furnished distannane **8** in 60% yield (Scheme II). Metalation reactions of **6** in which a deficiency of base or of chlorostannane electrophile was used also produced **8** as the exclusive or major tin-containing product, along with recovered **6**. This unanticipated result suggested that a local concentration effect of the base or that its state of aggregation was inhibiting the formation of monometalated anthracene.[17] At the temperature at which the metalation reactions were conducted, it was clear that the rate of metalation was competitive with the rate at which the alkyllithium aggregate was being broken by the solvent. An alternative option would have been to slow the metalation by lowering the reaction temperature; however, this was precluded by the low solubility of the anthracene derivatives. The monostannylation of **6** was accomplished in 70% yield by treatment of an ethereal solution of 1.0 equiv of **6** at 25 °C with 1.3 equiv of *n*-butyllithium, which had been diluted to one-third of its initial concentration with hexane and 2.0 equiv of *N,N,N',N'*-tetramethylethylenediamine (TMEDA), followed by quenching with 1.0 equiv of tributylchlorostannane. Alternatively, dilution of a pentane solution of *tert*-butyllithium with ether at −10 °C prior to addition to an ethereal solution of **6**, followed by quenching with 1.3 equiv of tributylchlorostannane, produced monostannane **9** in 74% yield. Stannane **9** was iodinated in 94% yield by treatment with freshly sublimed iodine in dichloromethane to produce **10**. The meta-

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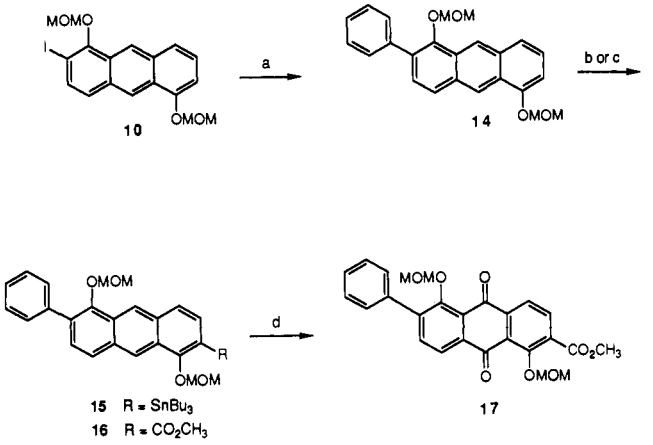
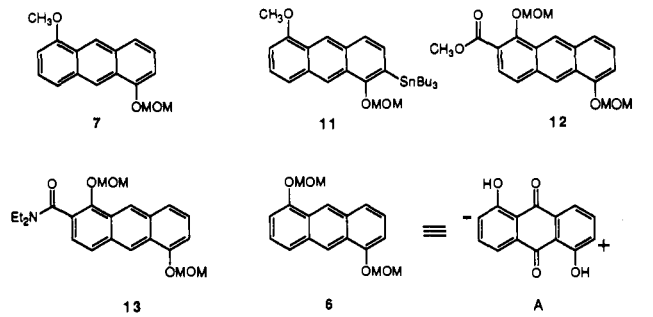
Scheme III[a]



[a] Key: (a) PhZnCl, THF, Pd(0), 25 °C, 73%; (b) (i) *n*-BuLi, TMEDA, THF, (ii) $ClCO_2CH_3$, 60% of **16**; (c) (i) *n*-BuLi, TMEDA, THF, (ii) *n*-Bu_3SnCl, 71% of **15**; (d) bis(pyridine)silver permanganate, silica gel, CH_2Cl_2, 85%.

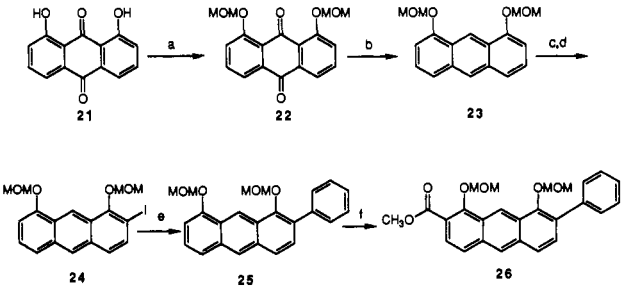
lation/stannylation reaction was repeated with anthracene **7** to produce monostannane **11** in 72% yield. Metalation/stannylation of **7** even without prior dilution of the base produced exclusively monostannane **11** in 72% yield, thus demonstrating that control over the site of metalation can be exercized by choice of the groups on oxygen. In all cases, chromatographic purification of the arylstannanes was conducted on silica gel that had been pretreated with 2% triethylamine in hexanes in order to inhibit acid-catalyzed destannylation.



The lithioanthracenes prepared by the methods described above could be trapped with reactive electrophiles. For example, the lithioanthracene derived from **6** was quenched with methyl chloroformate to produce **12** in 78% yield. Although the lithiated anthracenes could be derived from direct deprotonation, they were more conveniently generated from the corresponding stannanes, since the transmetalation reaction with *n*-butyllithium was both clean and quantitative. The lithioanthracenes were not very aggressive nucleophiles, and the substitution reaction was limited to the combination with highly reactive electrophiles. Diethylcarbamoyl chloride was very sluggish and reacted with the anion derived from **9** only at 55 °C in THF to produce **13** in 73% yield. Even more surprising, allylic bromides failed to undergo appreciable reaction in the absence of additives.[18]

The attenuated reactivity of the anthryllithiums was not an impediment. Iodoanthracene **10** provided an alternative for carbon–carbon bond formation. Efficient substitution of the anthracene nucleus was accomplished through the palladium-catalyzed coupling reaction[19] of **10** with organozinc halides. The complementary reactivities of the anthryllithiums derived from **9** and iodoanthracene **10** suggested that **6** could function as the synthetic equivalent of the hypothetical reagent A. In point of fact, by choice of the sequence of reactions, carbon atoms C2 and C6 can function as either electrophilic or nucleophilic centers in

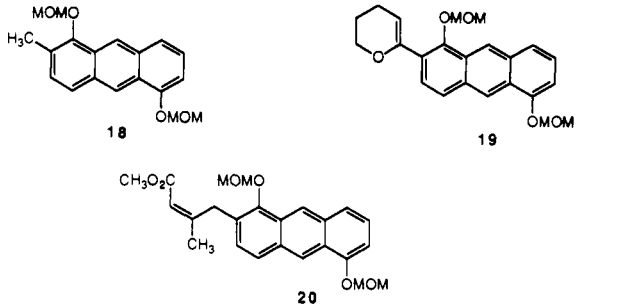
Scheme IV[a]



[a] Key: (a) CH_3OCH_2Cl, *i*-Pr_2NEt, $CHCl_3$, reflux, 100%; (b) $NaBH_4$ (excess), *i*-PrOH, reflux, 67%; (c) (i) *n*-BuLi, TMEDA, Et_2O, 25 °C, (ii) *n*-Bu_3SnCl, 83%; (d) I_2, CH_2Cl_2, 100%; (e) PhZnCl, THF, Pd(0), 25 °C, 62%; (f) (i) *n*-BuLi, TMEDA, THF, −10 °C, (ii) $ClCO_2CH_3$, 60%.

any combination. This is demonstrated in Scheme III. Palladium(0)-catalyzed coupling of iodoanthracene **10** with phenylchlorozinc, prepared from phenyllithium and freshly fused zinc chloride, in THF at 25 °C produced **14** in 73% yield. Subsequent metalation of **14** at −10 °C in THF with 2.5 equiv of *n*-butyllithium and 5.0 equiv of TMEDA, followed by quenching with methyl chloroformate, gave methyl ester **16** in 60% yield, along with 10–15% recovered **14**. Quenching the anion with tributylchlorostannane produced **15** in 71% yield. The oxidation of **16** to anthraquinone **17** was accomplished in 85% yield with bis(pyridine)silver permanganate.[15] It was essential that the heterogeneous residue from this oxidation reaction be extracted thoroughly with ethyl acetate in order to ensure a high yield of product.

The palladium-catalyzed reaction of iodoanthracene **10** with methylchlorozinc produced **18** in 62% yield. Particularly useful for the vineomycinone B2 synthesis was the coupling of **10** with



2-lithiodihydropyran[20] in the presence of zinc chloride. Product anthracene **19** (72% yield) was a model for the *C*-glycosyl portion of the natural product. In a parallel study, methyl senecioate was converted to its chlorozinc enolate by sequential treatment with lithium diisopropylamide (LDA) and zinc chloride. Palladium-catalyzed coupling to **10** produced methyl ester **20** as a single geometrical isomer in 33% yield. A strong nuclear Overhauser effect between the vinyl methyl and the vinyl hydrogen proved that **20** was obtained as the *Z* isomer. This is consistent with Weiler's interpretation:[21] the methoxycarbonyl group directed deprotonation of the *Z* methyl group to provide the internally chelated enolate, which determined the geometry of the double bond. Although the yield for the preparation of **20** was disappointing, it served as a model for the linear side chain of vineomycinone B2.

The reactions described in Schemes II and III have been duplicated with 1,8-dihydroxyanthraquinone (**21**) (Scheme IV). The selectivity for the monometalation/stannylation of **23** paralleled that of **6**. Yields for the reactions were in all cases comparable to those obtained in the anthrarufin series. This indicated general applicability of the procedures described. It should also be noted

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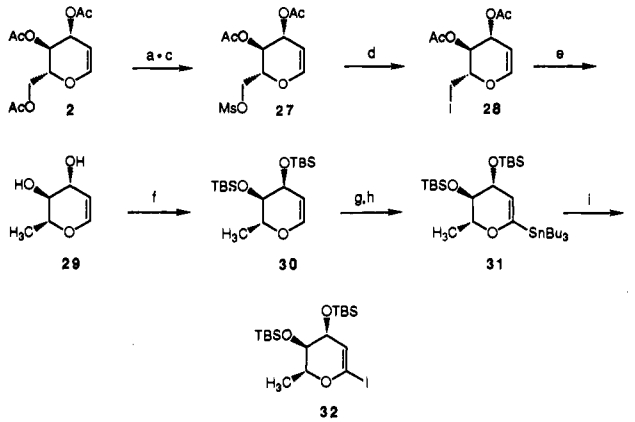
Scheme V[a]



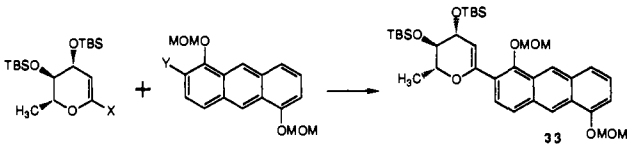
[a] Key: (a) K_2CO_3, CH_3OH; (b) MsCl, Et_3N; (c) $(CH_3CO)_2O$, pyridine, 52% overall from **2**;[22] (d) LiI, THF, reflux, 80–95%; (e) LAH, THF, 25 °C, 92%; (f) TBSOTf, Et_3N, CH_2Cl_2, 96%; (g) *t*-BuLi, THF, pentane; (h) *n*-Bu_3SnCl, 92% from **30**; (i) I_2, CH_2Cl_2, 96%.

that the butoxymethoxyl directing group was briefly examined. Any advantage of the marginally greater solubility of these derivatives was offset by the greater complexity of their ^1H NMR spectra.

The results of the preliminary studies augured well for the success of the retrosynthetic scheme. The preparation of the olivose derivative was accomplished by modifying a published reaction sequence[22] proceeding from **2**. Hydrolysis of **2** with potassium carbonate in methanol followed by selective mesylation of the primary alcohol and reacetylation in a one-pot procedure provided **27** in 52% isolated yield (Scheme V). Exposure of **27** to anhydrous lithium iodide in refluxing THF provided **28** (80–95% yield), which was subsequently treated with lithium aluminum hydride (LAH) to produce **29** in 92% yield. Protection of **29** as the bis(*tert*-butyldimethylsilyl) ether was accomplished in 96% yield with *tert*-butyldimethylsilyl triflate and triethylamine in dichloromethane.[23] Metalation of **30** with *tert*-butyllithium in THF/pentane according to Boeckman's procedure,[20] followed by trapping with tributylchlorostannane, produced stannyl sugar **31**. Exposure of **31** to iodine in dichloromethane produced the corresponding iodo sugar **32** in 96% yield.

Two complementary approaches suggested themselves for the *C*-glycosyl coupling reaction. The metalloanthracene could undergo catalyzed coupling to the iodo sugar; alternatively, the metalated sugar could undergo reaction with the iodoanthracene. Both approaches were examined, and the results are summarized in Table I. The use of iodo sugar **32** (X = I, entries 1–5, Table I) was inconvenient for two reasons: (i) low recovery of **32** during chromatographic purification; (ii) neat **32** was unstable to storage and darkened perceptibly after a few minutes of exposure to air. Some coupling reactions were performed with **32**, but the conditions were not optimized. Much better results were obtained by using the sugar as the nucleophile (entries 6–13). The Grignard reagent derived from addition of anhydrous $MgBr_2$ in THF to the lithio sugar tended to decompose under the reaction conditions; notwithstanding, relatively high yields have been reported in related applications.[24] The low yields for entries 7–9 are consistent with published work; few coupling reactions of stannanes with haloaromatic compounds, mediated by palladium catalysts, proceed efficiently when the aromatic bears an electron-donating substituent ortho to the halogen atom.[25,26] The chlorozinc derivative

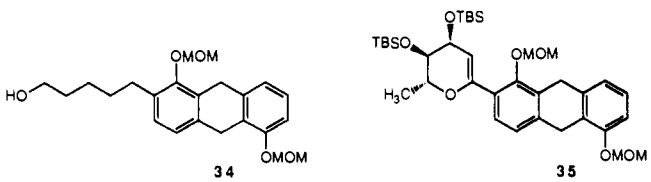
Table I. Preparation of **33** by Transition-Metal-Catalyzed Coupling



entry	X	Y	conditions	yield of **33**, %
1	I	MgBr	$Ni(dppp)Cl_2$; ether; reflux	12
2	I	ZnCl	$Ni(dppp)Cl_2$; ether; THF; 23 °C	32
3	I	ZnCl	$Pd(PPh_3)_2Cl_2$ + DIBAL; THF; 23 °C	0
4	I	$SnBu_3$	$Pd(CH_3CN)_2Cl_2$; DMF; 80 °C	0
5	I	$SnBu_3$	$Pd(CH_3CN)_2Cl_2$ + PPh_3; $CHCl_3$; 80 °C	0
6	MgBr	I	$Pd(PPh_3)_2Cl_2$ + DIBAL or $Ni(dppp)Cl_2$	0
7	$SnBu_3$	I	$Pd(CH_3CN)_2Cl_2$; DMF; 80 °C	31
8	$SnBu_3$	I	$Pd(CH_3CN)_2Cl_2$ + LiCl; DMF; 80 °C	15
9	$SnBu_3$	I	$Pd(PPh_3)_2Cl_2$ + LiCl; THF; 80 °C	19
10	ZnCl	I	$Ni(PPh_3)_2Cl_2$; THF; 80 °C	35
11	ZnCl	I	$Ni(dppp)Cl_2$; ether; 23 °C	52
12	ZnCl	I	$Ni(dppp)Cl_2$; THF; 23 °C	24
13	ZnCl	I	$Pd(PPh_3)_2Cl_2$ + DIBAL; THF; 23 °C	78.5

of the sugar was the nucleophile of choice for the preparation of **33**, and acceptable yields were obtained with $Ni(dppp)Cl_2$ as the catalyst.[27] The best procedure made use of the active palladium catalyst, which is generated by in situ reduction of $Pd(PPh_3)_2Cl_2$ by diisobutylaluminum hydride in THF.[19] Moreover, unreacted starting materials can be recycled, following chromatographic separation and purification of the product. It is noteworthy that, with careful exclusion of oxygen from the reaction mixture, the product of carbohydrate homocoupling is absent. All reactions of stannane **31** produced some of the sugar derived dimer.[28]

Following the successful formation of the anthracene *C*-glycosyl bond, the next task to be addressed was the stereospecific reduction of the styryl double bond. Anthracene **19** was used as a model for **33**. This step provided an unanticipated challenge. In spite of precedent that indicated the uneventful catalytic hydrogenation of related systems,[29] hydrogenation of **19** took place only under forcing conditions and then complicated mixtures of products were formed in which the central ring of the anthracene had undergone reduction. This suggested that the saturation of the central anthracene ring was faster than the reduction of the styrene, reflecting a combination of two factors: a hindered, slow-reacting carbon–carbon double bond and an easily reduced anthracene. Dissolving metal reductions were also unsuccessful when applied to **19**. Exposure of **19** to lithium or sodium in liquid ammonia and THF, in the presence of 2-methyl-2-propanol, led to dihydroanthracene **34**. At short reaction times **34** was accompanied



by unreacted **19** in the product mixture. This was a clear indication that partial saturation of the anthracene was followed by styryl bond reduction, and by an even faster cleavage of the

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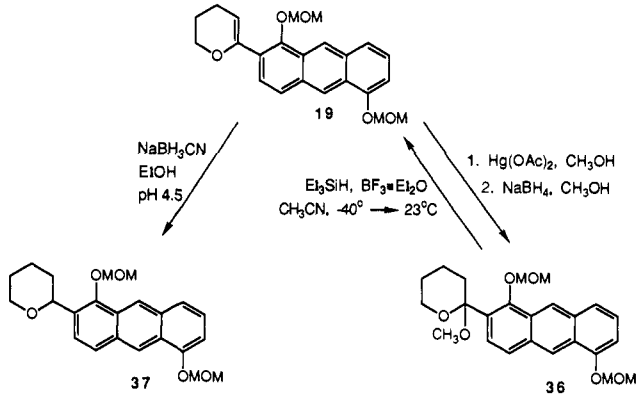
Scheme VI

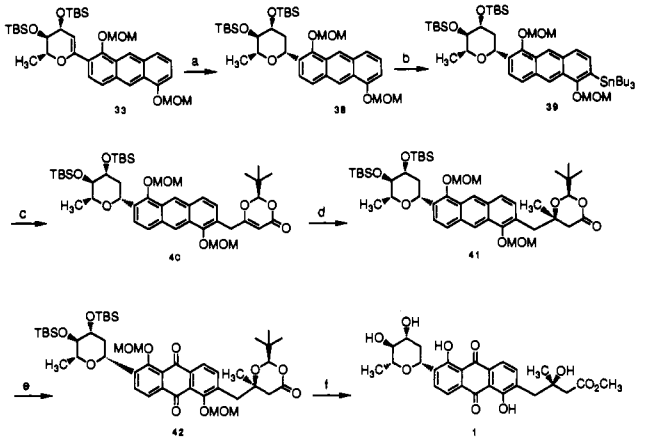


benzylic carbon–oxygen bond. It is noteworthy that **33** was converted to **35** in a very clean and completely selective reduction using metallic ytterbium.[30] The partial saturation of the anthracene nucleus would not constitute an obstacle to the total synthesis, so long as styrene reduction would take place, for the reoxidation to the quinone could be accomplished.

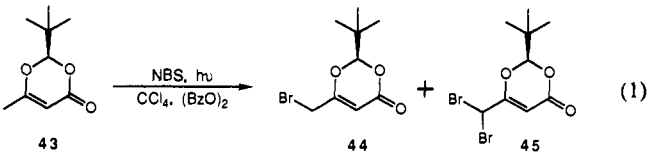
Because the styryl bond was electron rich, it was reasoned that one could attempt to form the oxygen-stabilized benzylic cation and then capture it with a hydride source. Treatment of **19** with triethylsilane and BF_3·Et_2O led to product mixtures in which cleavage of the pyran ring had taken place, suggesting that milder reaction conditions be examined. Oxymercuration/demercuration of **19** provided methoxy acetal **36** in 58% yield (unoptimized; Scheme VI). Exposure of **36** at −40 °C in acetonitrile and triethylsilane to BF_3·Et_2O cleanly produced **19**! This unexpected result suggested that the benzylic cation was indeed formed but that its collapse to **19** by proton loss was faster than its capture by hydride. This result also suggested the reaction conditions that were ultimately successful: The cation would have to be generated *reversibly* in the presence of a hydride source. In the event, careful alternate addition of methanolic HCl and $NaBH_3CN$ to a solution of **19** in ethanol at 25 °C led to pyran **37** in 58% yield.[31] The pH of the mixture was kept at approximately 4.5 by monitoring the color of bromocresol green, which had been added to the reaction mixture. Control of the pH was very important in order to avoid the loss of the oxygen protecting groups. It was gratifying to find that treatment of **33** under the same reaction conditions provided **38** in 87% yield as a single stereoisomer (Scheme VII). The higher yield in this case is a consequence of a more carefully optimized reaction. The stereochemistry for the reduction was the desired one with the anthracenyl group equatorial. This was shown by the positive NOE between the axial benzylic methine hydrogen and the methine hydrogen adjacent to the methyl on the sugar.

The final task was to introduce the five-carbon chain. The preparation of **20** during the model study and several related results[18] gave a good indication that the synthesis of vineomycinone B2 methyl ester could be brought to a successful conclusion. The low yield for **20** was of some concern; however, the balance of the material was recovered anthracene, so this approach would have been serviceable, though inelegant. Although the asymmetric center on the side chain could have been introduced through a straightforward application of the Sharpless epoxidation, this would inevitably detract from the overall convergency of the synthesis. By taking advantage of the elegant work by Seebach,[32] a much more efficient synthesis was achieved. Allylic bromination of **43** with *N*-bromosuccinimide and catalytic benzoyl peroxide in CCl_4 under irradiation by a floodlamp gave monobromide **44** in 42% yield, along with dibromide **45** (17% yield) and ca. 17% recovered **43** (eq 1). The chromatographic separation of these materials was tedious, but was readily accomplished.

Scheme VII[a]



[a] Key: (a) $NaBH_3CN$, HCl, EtOH, 87%; (b) *n*-BuLi, TMEDA, THF, 0 °C, then *n*-Bu_3SnCl, 92%; (c) **44**, $Pd_2(dba)_3$·$CHCl_3$, PPh_3, THF, 70 °C, 48 h, 45–50%; (d) $(CH_3)_2CuLi$, Et_2O, 51% + 25% **40**; (e) bis(pyridine)silver permanganate, silica gel, CH_2Cl_2, 85%; (f) HCl, CH_3OH, 23 °C, 76%.



(1)

Anthracene **38** was lithiated with *n*-butyllithium in the presence of TMEDA and was converted to tributylstannane **39** (92% yield) in a single operation. Treatment of an equimolar mixture of monobromide **44** and stannane **39** with 0.06 equiv of $Pd_2(dba)_3$·$CHCl_3$ and 0.12 equiv of triphenylphosphine[33] in THF at 70 °C for 48 h, with scrupulous exclusion of air, afforded **40** in 45–50% yield along with ca. 15% of **38**. The stereogenic center on the side chain was introduced by addition of lithium dimethylcuprate[32] to **40** (51% yield and 25% recovered starting material). Product **41** was obtained as a single diastereoisomer, as indicated by ^1H NMR at 300 MHz. This result was confirmed by ^1H NMR at 500 MHz of **42**. Danishefsky and co-workers have reported that *epi*-vineomycinone B2 methyl ester is distinguishable from vineomycinone B2 methyl ester by ^1H NMR at 500 MHz in deuteriochloroform.[7] The conversion of **41** to vineomycinone B2 methyl ester was accomplished in two steps. Oxidation with bis(pyridine)silver permanganate[15] in dichloromethane provided anthraquinone **42** in 85% yield. The lability of the protective groups, which had been a small inconvenience at some points of the sequence, was used to our advantage at this junction: All protecting groups were removed in a single operation by exposure of **42** to HCl in anhydrous methanol at 23 °C for 4 h to provide methyl ester **1** in 64% overall yield from **41** as a single isomer. The overall yield for these last steps is significantly higher than in our preliminary report.[10] This is a consequence of conducting the reactions on a larger scale. The synthetic material was identical with an authentic sample by spectroscopic comparison and by optical rotation. It should be noted that the values for the optical rotation were found to be very sensitive to concentration.

Conclusion

A triply convergent total synthesis of the *C*-glycosylanthraquinone antibiotic vineomycinone B2 methyl ester has been described. A general methodology for appending *C*-glycosyl units onto anthraquinones and anthracenes has been described and can be used for the preparation of diverse *C*-glycosides. The availa-

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bility of hydroxyanthraquinones suggests that this methodology will be suitable for the synthesis of other, more complex members to this family of natural products.

Experimental Section

All reactions were performed in flame-dried glass apparatus equipped with rubber septa under a static nitrogen or argon atmosphere. Thin-layer chromatography was performed on EM Reagents precoated silica gel 60 F-254 analytical plates (0.25 mm). Flash chromatography was performed on Brinkmann silica gel (0.043–0.063 mm). Melting points were reported for all crystalline products. All other products were isolated as clear oils. Elemental analyses were performed by MicAnal (Tucson, AZ).

Proton nuclear magnetic resonance spectra were recorded at 300 MHz on a GE QE300 spectrometer (Oxford magnet) or at 500 MHz on a GE QE500 spectrometer. NMR data are recorded (ppm) vs $CHCl_3$ (7.26 ppm). Infrared spectra were recorded on a Perkin-Elmer IR 1430 spectrometer. Electron-impact mass spectra were performed on a VG-70SE mass spectrometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter.

Hydroxyanthraquinone Protection, 1,5-Bis(methoxymethoxy)-9,10-anthraquinone (4). A suspension of 1.00 g (4.2 mmol) of anthrarufin in 15 mL of chloroform was treated with 13.5 mL (77.6 mmol) of *N,N*-diisopropylethylamine and 8.0 mL (ca. 51.2 mmol) of a 6.4 M solution of chloromethyl methyl ether[34] at 23 °C and was subsequently heated to reflux for 16 h. The mixture was allowed to cool to 23 °C and was washed with 1 N aqueous NaOH until the washings were pale pink, followed by brine. The organic phase was dried over $MgSO_4$, and the solvent was evaporated. The resulting solid was washed successively with 1 N NaOH, water, and absolute ethanol to afford 1.00 g of anthraquinone **4** as a yellow solid (73% yield): mp 209–211 °C; IR (neat thin film deposited on NaCl from CH_2Cl_2) 1670, 1160, 1090 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.93 (d, J = 7.7 Hz, 2 H), 7.65 (dd, J = 8.3, 7.7 Hz, 2 H), 7.50 (d, J = 8.3 Hz, 2 H), 5.37 (s, 4 H), 3.55 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 182.54, 159.75, 137.49, 134.91, 121.06, 119.71, 116.81, 95.43, 56.50 ppm; mass spectrum, m/e 328 (M^+), 284, 253, 240 (100%), 224; exact mass calcd for $C_{18}H_{16}O_6$ 328.0947, found 328.0967. Anal. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.70; H, 4.97.

1-(Methoxymethoxy)-5-methoxy-9,10-anthraquinone. From 431 mg (1.70 mmol) of 1-methoxy-5-hydroxy-9,10-anthraquinone[35] was obtained 400 mg of 1-(methoxymethoxy)-5-methoxy-9,10-anthraquinone (79% yield): mp 187–188 °C; IR (neat thin film deposited on NaCl from CH_2Cl_2) 1660, 1590, 1265 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.96 (d, J = 7.6 Hz, 1 H), 7.90 (d, J = 7.8 Hz, 1 H), 7.68 (m, 2 H), 7.50 (d, J = 8.4 Hz, 1 H), 7.28 (d, J = 8.4 Hz, 1 H), 5.39 (s, 2 H), 4.04 (s, 3 H), 3.57 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 182.44, 159.70, 157.07, 137.31, 137.22, 134.96, 134.73, 121.18, 121.03, 119.56, 116.76, 95.17, 56.52, 56.45 ppm; mass spectrum, m/e 298 (M^+), 283, 266, 254, 238 (100%); exact mass calcd for $C_{17}H_{14}O_5$ 298.0841, found 298.0847.

1,8-Bis(methoxymethoxy)-9,10-anthraquinone (22). This material (6.8 g) was prepared in quantitative yield from 5.0 g (20.8 mmol) of 1,8-dihydroxy-9,10-anthraquinone according to the general procedure described for **4**. Two recrystallizations from ethyl acetate produced an analytically pure sample: mp 148–150 °C; IR (neat thin film deposited on NaCl from CH_2Cl_2) 2950, 1670, 1590, 1320 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.94–7.91 (m, 2 H), 7.65–7.55 (m, 4 H), 5.38 (s, 4 H), 3.57 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 183.35, 182.28, 156.73, 134.50, 133.57, 124.80, 122.56, 120.27, 95.14, 56.30 ppm; mass spectrum, m/e 328 (M^+), 297, 283, 253; exact mass calcd for $C_{18}H_{16}O_6$ 328.0947, found 328.0937. Anal. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.53; H, 4.86.

Anthraquinone Reduction, 1,5-Bis(methoxymethoxy)anthracene (6). To a suspension of 2.56 g (7.8 mmol) of anthraquinone **4** in 125 mL of 2-propanol was added 9.00 g (ca. 237 mmol) of $NaBH_4$. The mixture was heated to reflux for 8 h, poured onto ice water, and treated slowly with 6 N HCl at 0 °C until the pH of the mixture was 4–6. The solid anthracene was filtered, and the aqueous fraction was extracted with CH_2Cl_2. The organic phase was washed with water and dried over $MgSO_4$, and the solvent was evaporated to produce additional crude anthracene as a yellow-brown solid. Flash column chromatography of the combined solids gave 2.02 g (87% yield) of **6** as a pale yellow solid: mp 130–133 °C; IR (neat thin film deposited on NaCl from CH_2Cl_2) 1150, 1075, 1055, 980 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.80 (s, 2 H), 7.69 (d, J = 8.6 Hz, 2 H), 7.36 (dd, J = 8.6, 7.4 Hz, 2 H), 7.03 (d, J = 7.4 Hz, 2 H), 5.48 (s, 4 H), 3.60 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 152.71, 132.28, 125.39, 125.09, 122.12, 120.49, 105.96, 94.75, 56.33 ppm; mass spectrum, m/e 298 (M^+, 100%), 268, 253, 238, 223; exact mass calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1199. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.49; H, 6.14.

1-(Methoxymethoxy)-5-methoxyanthracene (7). Reduction of 267 mg (0.90 mmol) of the anthraquinone afforded 147 mg of anthracene **7** (61% yield): mp 122–125 °C; IR (neat thin film deposited on NaCl from CH_2Cl_2) 1625, 1540, 1465, 1250, 1150, 1110, 985, 950, 885 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.79 (br s, 2 H), 7.69 (d, J = 8.5 Hz, 1 H), 7.63 (d, J = 8.5 Hz, 1 H), 7.35 (m, 2 H), 7.03 (d, J = 7.4 Hz, 1 H), 6.74 (d, J = 7.4 Hz, 1 H), 5.48 (s, 2 H), 4.08 (s, 3 H), 3.60 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 157.67, 155.28, 152.67, 132.20, 125.40, 125.21, 125.09, 124.94, 122.18, 120.96, 120.61, 120.27, 105.95, 101.88, 94.71, 56.28, 55.41 ppm; mass spectrum, m/e 268 (M^+, 100%), 238, 223, 195, 180, 152; exact mass calcd for $C_{17}H_{16}O_3$ 268.1099, found 268.1104.

1,8-Bis(methoxymethoxy)anthracene (23). Reduction of 5.0 g (15.2 mmol) of anthraquinone **22** afforded 3.0 g of anthracene **23** as a pale yellow solid (67% yield): mp 64–65 °C; IR (neat thin film deposited on NaCl from CH_2Cl_2) 2950, 1625, 1560, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 9.24 (s, 1 H), 8.35 (s, 1 H), 7.63 (d, J = 9.0 Hz, 2 H), 7.37 (t, J = 9.0 Hz, 2 H), 7.05 (d, J = 9.0 Hz, 2 H), 5.50 (s, 4 H), 3.61 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 153.14, 132.76, 125.47, 125.41, 124.62, 121.26, 115.39, 105.60, 94.58, 56.08 ppm; mass spectrum, m/e 298 (M^+), 266, 236; exact mass calcd for $C_{18}H_{18}O_4$ 298.1205, found 298.1218. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.45; H, 6.10.

Anthracene Metalation/Stannylation, Stannane 9. *tert*-Butyllithium (9.5 mL of a 1.7 M solution in pentane, 16.15 mmol) was diluted with 25 mL of ether at −10 °C and transferred via cannula to a solution of 1.27 g (4.26 mmol) of anthracene **6** in 90 mL of ether at 23 °C. After 2 h the mixture was treated with 5.0 mL (18.43 mmol) of tributylchlorostannane and was allowed to react for 45 min. The reaction was quenched by the addition of water, the organic phase was washed with saturated aqueous NaCl and dried over $MgSO_4$, and the solvent was evaporated. Flash column chromatography on silica gel that had been pretreated with 1–2% triethylamine in hexane, eluting with the same solvent, produced 1.84 g of **9** as a clear oil (74% yield).

Alternative Procedure for Metalation/Stannylation. To 1.7 mL of a 1.4 M solution of *n*-butyllithium (2.38 mmol) in hexanes were added 5.1 mL of hexanes and 0.6 mL (3.98 mmol) of TMEDA. The resulting mixture was added dropwise over a 20-min period to a solution of 600 mg (2.01 mmol) of anthracene **6** in ca. 40 mL of ether. The reaction mixture was stirred for 2 h at 23 °C and 0.65 mL (2.39 mmol) of tributylchlorostannane was added. Aqueous workup and flash column chromatography on silica gel that had been pretreated with 1–2% triethylamine in hexane, eluting with the same solvent, produced 825 mg (70% yield) of **9** and 15% of unreacted **6**. Stannane 9: ^1H NMR (300 MHz, $CDCl_3$) 8.83 (s, 1 H), 8.73 (s, 1 H), 7.82 (d, J = 8.4 Hz, 1 H), 7.69 (d, J = 8.4 Hz, 1 H), 7.44 (d, J = 8.3 Hz, 1 H), 7.35 (dd, J = 8.4, 7.4 Hz, 1 H), 7.02 (d, J = 7.4 Hz, 1 H), 5.48 (s, 2 H), 5.20 (s, 2 H), 3.68 (s, 3 H), 3.60 (s, 3 H), 1.59 (m, 6 H), 1.38 (m, 6 H), 1.16 (m, 6 H), 0.90 (t, J = 7.3 Hz, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 125.29, 125.13, 124.74, 122.35, 120.92, 120.83, 105.89, 100.55, 94.75, 57.75, 56.33, 29.19, 27.42, 13.69, 10.43 ppm.

Stannane 11. To a solution of 323 mg (1.21 mmol) of anthracene **7** in 15.0 mL of ether at −10 °C was added 2.9 mL (4.90 mmol) of a 1.7 M solution of *tert*-butyllithium in pentane. The reaction mixture was stirred at 23 °C for 2 h, and 1 equiv of tributylchlorostannane was added. After 45 min aqueous workup followed by flash column chromatography on silica gel that had been pretreated with 2% triethylamine in hexane produced 489 mg (72% yield) of stannane **11** as an oil: IR (neat) 1610, 1555, 1525, 1460, 1160, 1080, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.81 (s, 1 H), 8.71 (s, 1 H), 7.81 (d, J = 8.3 Hz, 1 H), 7.63 (d, J = 8.6 Hz, 1 H), 7.43 (d, J = 8.3 Hz, 1 H), 7.33 (dd, J = 8.3, 7.4 Hz, 1 H), 6.74 (d, J = 7.4 Hz, 1 H), 5.20 (s, 2 H), 4.08 (s, 3 H), 3.69 (s, 3 H), 1.60 (m, 6 H), 1.36 (m, 6 H), 1.19 (m, 6 H), 0.90 (t, J = 7.3 Hz, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 158.98, 155.33, 133.30, 132.53, 131.83, 129.22, 126.87, 125.13, 125.00, 124.84, 121.20, 120.99, 120.72, 101.80, 100.52, 57.71, 55.45, 29.19, 27.41, 13.67, 10.42 ppm.

2-(Tributylstannyl)-1,8-bis(methoxymethoxy)anthracene. A solution of 600 mg (2.00 mmol) of anthracene **23** was dissolved in ca. 35 mL of ether. A solution of *n*-butyllithium (2.0 mL of a 1.04 M solution in hexanes, 2.08 mmol) was diluted with 6.0 mL of hexanes and 0.6 mL of TMEDA. The butyllithium solution was added to the anthracene during 15–20 min. The reaction mixture was allowed to stir for 2 h at 23 °C following which 0.54 mL of tributylchlorostannane (2.00 mmol) was added. After 30 min, aqueous workup followed by flash column chromatography produced 1.0 g of the stannane (83% yield) as a pale yellow oil: IR (neat) 2955, 2920, 2860, 1630, 1610, 1560 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 9.22 (s, 1 H), 8.37 (s, 1 H), 7.76 (d, J = 9.0 Hz, 1 H),

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7.62 (d, J = 9.0 Hz, 1 H), 7.46 (d, J = 9.0 Hz, 1 H), 7.35 (t, J = 9.0 Hz, 1 H), 7.00 (d, J = 9.0 Hz, 1 H), 5.47 (s, 2 H), 5.22 (s, 2 H), 3.74 (s, 3 H), 3.60 (s, 3 H), 1.62–1.54 (m, 6 H), 1.40–1.30 (m, 6 H), 1.21–1.16 (m, 6 H), 0.90 (t, J = 7.2 Hz, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 159.81, 153.23, 133.87, 132.72, 132.50, 128.75, 126.37, 125.63, 125.50, 124.98, 124.05, 121.30, 116.20, 105.54, 100.78, 94.71, 57.65, 56.30, 29.19, 27.43, 13.71, 10.40 ppm.

Stannane Iodination. 2-Iodo-1,5-bis(methoxymethoxy)anthracene (10). A solution of sublimed iodine (677 mg, 2.67 mmol) in 30 mL of CH_2Cl_2 was added via cannula to a solution of 1.426 g (2.43 mmol) of stannane **9** in 8.0 mL of CH_2Cl_2 at 23 °C. After the mixture was stirred for 10 min, a saturated aqueous solution of $NaHSO_3$ was added and the mixture was extracted with CH_2Cl_2. The organic phase was washed with water and saturated aqueous NaCl and dried ($MgSO_4$), and the solvent was evaporated. Flash column chromatography on silica gel afforded 974 mg of **10** (94% yield): mp 68–69 °C; IR (neat) 2960, 1615, 1532, 1460 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.82 (s, 1 H), 8.68 (s, 1 H), 7.70 (m, 2 H), 7.60 (d, J = 9.0 Hz, 1 H), 7.40 (d, J = 7.4 Hz, 1 H), 7.06 (d, J = 7.4 Hz, 1 H), 5.47 (s, 2 H), 5.34 (s, 2 H), 3.81 (s, 3 H), 3.59 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 152.67, 134.11, 132.78, 131.99, 127.70, 126.74, 126.00, 125.54, 122.08, 121.35, 121.30, 120.95, 106.34, 100.32, 94.74, 86.68, 58.43, 56.36 ppm; mass spectrum, m/e 424 (M^+, 100%), 379, 297; exact mass calcd for $C_{18}H_{17}IO_4$ 424.0171, found 424.0162.

2-Iodo-1,8-bis(methoxymethoxy)anthracene (24). A solution of 500 mg (0.85 mmol) of 2-(tributylstannyl)-1,8-bis(methoxymethoxy)-anthracene in ca. 15 mL of CH_2Cl_2 was treated with a solution of 238 mg (0.94 mmol) of sublimed iodine in CH_2Cl_2 at 23 °C. The organic phase was washed with 5% aqueous $Na_2S_2O_3$ followed by water and saturated aqueous NaCl. Drying ($MgSO_4$) and concentration followed by flash column chromatography produced 360 mg of **24** (quantitative yield) as a yellow solid: mp 50–53 °C; IR (neat) 2960, 1610, 1560, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 9.18 (s, 1 H), 8.35 (s, 1 H), 7.73 (d, J = 9.0 Hz, 1 H), 7.62 (d, J = 9.0 Hz, 1 H), 7.54 (d, J = 9.0 Hz, 1 H), 7.42–7.37 (m, 1 H), 7.05 (d, J = 7.5 Hz, 1 H), 5.48 (s, 2 H), 5.36 (s, 2 H), 3.87 (s, 3 H), 3.59 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 154.89, 153.11, 134.56, 132.98, 132.55, 127.18, 126.17, 126.01, 125.25, 121.23, 116.35, 106.23, 100.58, 94.70, 86.14, 58.35, 56.32 ppm; mass spectrum, m/e 424 (M^+), 361, 247; exact mass calcd for $C_{18}H_{17}IO_4$ 424.0171, found 424.0135.

Reactions of Anthracene Anions with Electrophiles. 2-Carbomethoxy-1,5-bis(methoxymethoxy)anthracene (12). A solution of 825 mg (1.40 mmol) of stannane **9** in 15 mL of THF was cooled to −78 °C. To this solution was added 1.5 mL of n-butyllithium in hexanes (1.04 M, 1.56 mmol), and the reaction mixture was allowed to stir for 1 h at −78 °C. The reaction mixture was quenched by the addition of 740 mg (7.83 mmol) of freshly distilled methyl chloroformate in 2 mL of THF. Aqueous workup followed by flash column chromatography produced 390 mg of **12** as a yellow solid (78% yield): mp 80–82 °C; IR (neat) 2950, 1720, 1620, 1535 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.93 (s, 1 H), 8.83 (s, 1 H), 7.81–7.71 (m, 3 H), 7.43–7.38 (m, 1 H), 7.10 (d, J = 7.5 Hz, 1 H), 5.48 (s, 2 H), 5.35 (s, 2 H), 3.98 (s, 3 H), 3.69 (s, 3 H), 3.60 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 166.58, 156.22, 152.50, 133.24, 132.73, 127.53, 126.48, 125.76, 124.92, 124.54, 123.46, 122.20, 120.78, 117.69, 106.85, 101.94, 94.62, 57.97, 56.26, 52.13 ppm; mass spectrum, m/e 356 (M^+), 312, 280, 235; exact mass calcd for $C_{20}H_{20}O_6$ 356.1260, found 356.1280.

***N,N*-Diethylamide 13.** To a solution of 177 mg (0.30 mmol) of stannane **9** in 4 mL of THF was added a solution of 0.30 mL of n-butyllithium in hexanes (1.4 M, 0.42 mmol) at −40 °C. The reaction mixture was stirred at 23 °C for 45 min. The solution was subsequently cooled to −78 °C, treated with 0.11 mL (0.87 mmol) of diethylcarbamoyl chloride, and heated at 52–58 °C for 30 min. Aqueous workup followed by flash chromatography afforded 87 mg of **13** (73% yield) along with 13 mg (15% yield) of anthracene **6**. Amide **13**: IR (neat) 1645, 1635, 1150 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.85 (s, 1 H), 8.79 (s, 1 H), 7.86 (d, J = 8.8 Hz, 1 H), 7.70 (d, J = 8.5 Hz, 1 H), 7.40 (dd, J = 8.5, 7.4 Hz, 1 H), 7.30 (d, J = 8.7 Hz, 1 H), 7.07 (d, J = 7.4 Hz, 1 H), 5.48 (s, 2 H), 5.32 (s, 2 H), 3.75 (br s, 1 H), 3.63 (s, 3 H), 3.60 (s, 3 H), 3.58 (br s, 1 H), 3.30 (br s, 2 H), 1.32 (t, J = 7.1 Hz, 3 H), 1.07 (t, J = 7.1 Hz, 3 H) ppm; mass spectrum, m/e 397 (M^+), 367, 350, 322, 305, 280 (100%); exact mass calcd for $C_{23}H_{27}NO_5$ 397.1889, found 397.1880.

Catalyzed Reaction of Iodoanthracenes with Nucleophiles. 1,5-Bis(methoxymethoxy)-2-methylanthracene (18). Anhydrous $ZnCl_2$ (1.4 g, 10.27 mmol) was heated to 100 °C under vacuum for 1 h and then dissolved in 20 mL of anhydrous THF. The solution was cooled to −10 °C, and 6.9 mL of a 1.2 M solution of methyllithium (8.26 mmol) was added slowly. The reaction mixture was allowed to stir at 23 °C for 1 h. In a separate flask, 87 mg (0.12 mmol) of $Pd(PPh_3)_2Cl_2$ was stirred in 1 mL of THF and DIBAL in THF was added dropwise until a dark brown coloration appeared. Stirring was continued for 10–15 min at 23 °C. The methylchlorozinc solution was transferred to the catalyst solution via cannula, followed by a solution of 175 mg (0.41 mmol) of iodoanthracene **10** in 5 mL of THF. The reaction mixture was stirred for 3 h. Aqueous workup followed by flash column chromatography produced 80 mg of **18** (62% yield) along with 23 mg (19% yield) of anthracene **6**. Methylanthracene **18**: IR (neat) 2960, 1630, 1545 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.82 (s, 1 H), 8.60 (s, 1 H), 7.79 (d, J = 9.0 Hz, 1 H), 7.68 (d, J = 9.0 Hz, 1 H), 7.39–7.27 (m, 2 H), 7.03 (d, J = 9.0 Hz, 1 H), 5.47 (s, 2 H), 5.25 (s, 2 H), 3.73 (s, 3 H), 3.59 (s, 3 H), 2.53 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 152.73, 150.30, 132.67, 131.66, 129.03, 127.63, 125.42, 125.28, 124.91, 124.72, 121.95, 120.93, 120.03, 105.57, 99.78, 94.67, 57.75, 56.28, 16.83 ppm; mass spectrum, m/e 312 (M^+), 298, 267 (100%); exact mass calcd for $C_{19}H_{20}O_4$ 312.1362, found 312.1367.

Dihydropyran 19. A solution of 0.6 mL (6.59 mmol) of dihydropyran in 2.4 mL of THF at −78 °C was treated with 6.6 mL (12.5 mmol) of a 1.9 M solution of *tert*-butyllithium in pentane. The reaction mixture was warmed to 0 °C during 30 min. To this reaction mixture was added a solution of 5.40 g (ca. 39.7 mmol) of fused $ZnCl_2$ in 33 mL of THF, and the resulting mixture was stirred for 20 min at 23 °C. In a separate flask a solution of 100 mg (0.14 mmol) of $Pd(PPh_3)_2Cl_2$ in 6 mL of THF was treated with 0.35 mL (0.35 mmol) of a 1.0 M solution of DIBAL in THF until a clear brown solution was formed. The solution of the organozinc reagent was transferred to the solution of catalyst followed immediately by a solution of 257 mg (0.61 mmol) of iodoanthracene **10** in 10 mL of THF. After 8 h at 23 °C aqueous workup and flash column chromatography produced 168 mg of coupled product **19** as a pale yellow oil (72% yield): IR (neat) 2930, 1650, 1150 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.84 (s, 1 H), 8.81 (s, 1 H), 7.80 (d, J = 8.8 Hz, 1 H), 7.71 (d, J = 8.5 Hz, 1 H), 7.48 (d, J = 8.8 Hz, 1 H), 7.37 (dd, J = 8.5, 7.4 Hz, 1 H), 7.04 (d, J = 7.4 Hz, 1 H), 5.47 (s, 2 H), 5.38 (t, J = 3.5 Hz, 1 H), 5.32 (s, 2 H), 4.26 (t, J = 5.0 Hz, 2 H), 3.66 (s, 3 H), 3.60 (s, 3 H), 2.28 (m, 2 H), 1.99 (m, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 152.68, 150.32, 150.14, 132.71, 132.07, 127.89, 126.26, 125.40, 125.28, 124.33, 123.69, 122.14, 121.65, 120.58, 106.00, 102.43, 99.61, 94.70, 66.72, 57.94, 56.31, 22.33, 20.96 ppm; mass spectrum, m/e 380 (M^+), 348 (100%), 303, 280, 235; exact mass calcd for $C_{23}H_{24}O_5$ 380.1624, found 380.1633.

Methyl Ester 20. A solution of 570 mg (5.00 mmol) of methyl senecioate in 15 mL of THF was treated for 45 min at −78 °C with 1.2 equiv of LDA. In a separate flask, a solution of 955 mg (7.10 mmol) of freshly fused $ZnCl_2$ in 10 mL of THF was prepared and was cooled to −10 °C. The anion solution was transferred to the $ZnCl_2$ via cannula, and the mixture was stirred for 1 h at −5 to 0 °C. A suspension of 35 mg (0.05 mmol) of $Pd(PPh_3)_2Cl_2$ in 1 mL of THF was treated with DIBAL in THF until a clear dark brown solution was obtained, and the solution was stirred for an additional 10–15 min. The solution of the zincate was transferred to the catalyst followed by the addition of a solution of 212 mg (0.50 mmol) of iodoanthracene **10** in 5 mL of THF. The reaction mixture was stirred overnight at 23 °C. The reaction mixture was partitioned between ether and water and dried ($MgSO_4$), and the solvent was evaporated. Flash column chromatography produced 68 mg (33% yield) of **20** as an oil and 25% of recovered anthracene **6**. Ester **20**: IR (neat) 2920, 1710, 1645 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.81 (s, 1 H), 8.60 (s, 1 H), 7.78 (d, J = 9.0 Hz, 1 H), 7.67 (d, J = 9.0 Hz, 1 H), 7.40–7.27 (m, 2 H), 7.02 (d, J = 9.0 Hz, 1 H), 5.89 (s, 1 H), 5.47 (s, 2 H), 5.26 (s, 2 H), 4.40 (s, 2 H), 3.77 (s, 3 H), 3.72 (s, 3 H), 3.59 (s, 3 H), 1.79 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 167.04, 158.37, 152.70, 150.81, 132.69, 131.87, 127.45, 127.00, 126.40, 125.45, 124.99, 121.97, 121.05, 120.50, 117.22, 105.79, 100.24, 94.67, 57.87, 56.32, 51.02, 32.74, 24.46 ppm; mass spectrum, m/e 410 (M^+), 334, 277. Anal. Calcd for $C_{24}H_{26}O_6$: C, 70.23; H, 6.38. Found: C, 69.52, H, 6.51.

1,8-Bis(methoxymethoxy)-2-phenylanthracene (25). A solution of 1.0 g (7.43 mmol) of freshly fused $ZnCl_2$ in 20 mL of THF was cooled to −10 °C and was treated with 7.5 mL of a 0.84 M solution (6.25 mmol) of phenyllithium. The mixture was allowed to stir for 1 h at 23 °C. In a separate flask, a suspension of 66 mg (0.09 mmol) of $Pd(PPh_3)_2Cl_2$ in 2 mL of THF was treated with DIBAL in THF until a clear brown solution was obtained. Stirring was continued for 10–15 min at 23 °C. The solution of phenylchlorozinc was transferred to the catalyst solution followed by the addition of a solution of 265 mg (0.62 mmol) of iodoanthracene **24** in 5 mL of THF. The reaction mixture was stirred for 3–4 h at 23 °C and partitioned between ether and water. The ether phase was washed with saturated aqueous NaCl and dried ($MgSO_4$), and the solvent was evaporated. Flash column chromatography produced 135 mg (62% yield) of **25** as an oil along with 5–7% of anthracene **23**. Phenylanthracene **25**: IR (neat) 3050, 2960, 2820, 1625, 1600, 1560 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 9.29 (s, 1 H), 8.40 (s, 1 H), 7.85 (d, J = 9.0 Hz, 1 H), 7.72–7.36 (m, 8 H), 7.05 (d, J = 9.0 Hz, 1 H), 5.49 (s, 2 H),

4.93 (s, 2 H), 3.59 (s, 3 H), 3.32 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 153.05, 150.20, 139.09, 132.81, 132.53, 129.69, 128.52, 128.36, 127.23, 127.02, 125.73, 125.64, 125.56, 125.32, 124.41, 121.33, 116.37, 105.82, 105.73, 99.71, 94.62, 57.50, 56.23 ppm; mass spectrum, *m/e* 374 (M^+), 342, 298; exact mass calcd for $C_{24}H_{22}O_4$ 374.1518, found 374.1526.

2-Carbomethoxy-1,8-bis(methoxymethoxy)-7-phenylanthracene (26). A solution of 100 mg (0.27 mmol) of phenylanthracene **25** in 5 mL of THF was cooled to −10 °C and treated with 0.41 mL of TMEDA followed by 1.3 mL of a 1.04 M solution (1.35 mmol) of *n*-butyllithium. The reaction mixture was stirred for 1 h at −10 °C, then cooled to −78 °C, and treated with a solution of 140 mg (1.48 mmol) of methyl chloroformate in 1 mL of THF. The reaction was quenched after 15 min by pouring onto saturated aqueous NaCl. The reaction mixture was partitioned between ether and water and dried ($MgSO_4$), and the solvent was evaporated. Flash column chromatography produced 70 mg (60% yield) of **26** as a pale yellow oil: IR (neat) 2940, 1720, 1620, 1600, 1560 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 9.47 (s, 1 H), 8.39 (s, 1 H), 7.85–7.70 (m, 4 H), 7.57–7.38 (m, 5 H), 5.39 (s, 2 H), 4.95 (s, 2 H), 4.00 (s, 3 H), 3.75 (s, 3 H), 3.29 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 166.61, 156.89, 150.36, 138.83, 133.84, 133.67, 131.37, 129.84, 129.65, 129.24, 128.41, 127.88, 127.53, 127.19, 125.95, 125.53, 124.18, 123.87, 119.68, 117.70, 102.14, 99.73, 58.05, 57.62, 52.22 ppm; mass spectrum, *m/e* 432 (M^+), 388, 356, 324; exact mass calcd for $C_{26}H_{24}O_6$ 432.1573, found 432.1555.

Preparation of the Sugar Fragment, 6-Deoxyglucal (29). A solution of 7.1 g (20.9 mmol) of iodoglucal **28** in 20 mL of THF was added to 114.0 mL of a 1.0 M solution of LAH in THF at 23 °C. After 2 h, the reaction mixture was treated with 54.5 g of NaF (1.30 mol) and water (23.9 mL in 75 mL of THF, slow addition at 0 °C). The resulting suspension was stirred for 1 h at 23 °C and filtered through a Celite pad, the solids were washed with THF, and the solvent was evaporated to afford 2.5 g (92% yield) of **29** as an off-white solid, which was not purified: IR (neat) 3300 (br), 1650, 1230, 1050 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 6.32 (d, J = 6.1 Hz, 1 H), 4.72 (dd, J = 6.1, 3.5 Hz, 1 H), 4.21 (m, 1 H), 3.44 (m, 1 H), 3.33 (m, 1 H), 2.30 (d, J = 3.5 Hz, exchanges with D_2O, 1 H), 1.79 (d, J = 6.4 Hz, exchanges with D_2O, 1 H), 1.39 (d, J = 6.3 Hz, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 144.73, 102.72, 75.46, 74.48, 70.36, 17.16 ppm; mass spectrum, *m/e* 130 (M^+), 113, 97, 86, 73 (100%), 58; exact mass calcd for $C_6H_{10}O_3$ 130.0630, found 130.0645.

Protected Glucal 30. To a solution of 2.50 g (19.2 mmol) of crude glucal **29** and 11.4 mL (81.79 mmol) of triethylamine in 40 mL of CH_2Cl_2 at 0 °C was added 11.3 mL (13.08 g, 49.55 mmol) of *tert*-butyldimethylsilyl triflate. After the reaction mixture was stirred at 23 °C for 1.5 h, the solvent was removed under vacuum and dry ether was added to the residue. Filtration through a Florisil pad with ether as the eluent produced 6.62 g (96% yield) of **30** as a clear oil. A sample for analysis was purified by flash column chromatography: IR (neat) 3070, 2960, 2920, 2860, 1650, 1470, 1460, 1250, 1110, 1070 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 6.29 (d, J = 6.1 Hz, 1 H), 4.66 (dd, J = 6.1, 3.5 Hz, 1 H), 4.08 (m, 1 H), 3.94 (m, 1 H), 3.56 (m, 1 H), 1.32 (d, J = 6.7 Hz, 3 H), 0.93 (br s, 18 H), 0.11 (s, 3 H), 0.10 (s, 6 H), 0.09 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 143.09, 133.60, 102.69, 75.18, 74.83, 69.27, 26.05, 25.98, 17.16, −3.70, −3.90, −4.10, −4.24 ppm; mass spectrum, *m/e* (no M^+), 343, 301 (100%), 172, 147, 115, 73.

Glucal Stannylation, Stannyl Sugar 31. A solution of 97 mg (0.27 mmol) of **30** in 0.2 mL of THF was treated at −78 °C with 0.3 mL (0.51 mmol) of a 1.7 M solution of *tert*-butyllithium in pentane. The mixture was warmed to 0 °C and was stirred for 30 min before quenching with 0.2 mL (0.70 mmol) of tributylchlorostannane. After 15 min, aqueous workup and chromatography on neutral alumina afforded 162 mg (92% yield) of stannane **31** as a labile clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) 4.67 (d, J = 2.7 Hz, 1 H), 4.10 (m, 1 H), 3.74 (m, 1 H), 3.48 (m, 1 H), 1.52 (m, 12 H), 1.30 (m, 18 H), 0.91 (s, 9 H), 0.89 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H), 0.08 (s, 3 H) ppm.

Glucal Iodination, Iodo Sugar 32. A solution of 179 mg (0.28 mmol) of stannane **31** in 2.0 mL of CH_2Cl_2 at 0 °C was treated with a solution of 88 mg (0.35 mmol) of sublimed iodine in the same solvent. After 5 min, a saturated solution of $NaHSO_3$ was added. The organic phase was separated, washed with water and saturated aqueous NaCl, and dried ($MgSO_4$), and the solvent was evaporated to give 130 mg (96% yield) of the sensitive iodide **32** as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) 5.23 (d, J = 3.6 Hz, 1 H), 4.14 (m, 1 H), 3.97 (m, 1 H), 3.62 (m, 1 H), 1.37 (d, J = 6.8 Hz, 3 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H) ppm.

Preparation of the Side Chain Fragment 44. To a solution of 170 mg (1.0 mmol) of (*R*)-2-*tert*-butyl-6-methyl-1,3-dioxin-4*H*-one (**43**) and a catalytic amount of benzoyl peroxide in 15 mL refluxing dry CCl_4, irradiated by a floodlamp, was added 178 mg (1.0 mmol) of *N*-bromosuccinimide in small portions. The addition was complete in ca. 1.5 h. The progress of the reaction was followed by TLC. The reaction mixture was cooled to 23 °C, and the solid succinimide was removed by filtration. The solvent was evaporated from the filtrate, and the residue was chromatographed on a silica gel column eluting with hexane/ether/triethylamine (4/1/0.002) to produce 104 mg (42% yield) of monobromide **44**, 56 mg (17% yield) of dibromide **45**, and 29 mg (17% yield) of starting material **43**. Monobromide **44**: IR (neat) 3090, 3020, 2960, 2900, 2860, 1740, 1630, 1480, 1390, 1350, 1200, 1070, 960, 900 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 5.59 (s, 1 H), 5.11 (s, 1 H), 4.00 (d, J = 12.0 Hz, 1 H), 3.88 (d, J = 12.0 Hz, 1 H), 1.09 (s, 9 H) ppm; mass spectrum, *m/e* 250, 248 (M^+, very weak), 193, 191, 165, 163 (100%), 112, 84; exact mass calcd for $C_9H_{13}O_3Br$ 248.0048, found 248.0049; exact mass calcd for $C_4H_4O_2Br$ 162.9385, found 162.9390. Dibromide **45**: IR (neat) 3090, 3020, 2970, 2900, 1740, 1620, 1480, 1390, 1360, 1260, 1200, 1150, 1070, 970, 950, 900 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 6.01 (s, 1 H), 5.74 (s, 1 H), 5.16 (s, 1 H), 1.21 (s, 9 H) ppm; mass spectrum, *m/e* (no M^+), 273 (weak), 271 (weak), 269 (weak), 245, 243 (100%), 241, 192, 190, 164, 162, 135, 133, 122, 120, 107, 105, 87; exact mass calcd for $C_5H_3O_3Br_2$ 268.8469, found 268.8454; exact mass calcd for $C_4H_3O_2Br_2$ 240.8509, found 240.8504.

Anthracene to Sugar Coupling, Glucal 33. To a solution of glucal **30** (1.146 g, 3.2 mmol) in 14 mL of THF was added dropwise 3.2 mL of *tert*-butyllithium in pentane (1.5 M, 4.8 mmol) at −78 °C. The mixture was stirred at 0 °C for 30 min. A solution of 870 mg (6.4 mmol) of fused $ZnCl_2$ in 14 mL of THF was added to the sugar anion, and the reaction mixture was stirred for an additional 1 h at 23 °C. In another flask, 280 mg (0.40 mmol) of $Pd(PPh_3)_2Cl_2$ was suspended in 12 mL of THF and the mixture was treated with 1.2 mL of DIBAL (1.0 M, 1.2 mmol) in THF slowly at 0 °C to afford a clear dark brown solution of Pd(0) catalyst. Iodoanthracene **10** (848 mg, 2.0 mmol) in 12 mL of THF was transferred to the solution containing the catalyst. The solution of catalyst and **10** was stirred for 15 min, and the solution of zincate was transferred via cannula. The reaction mixture was stirred for 12 h at 23 °C. The reaction was quenched by adding saturated aqueous NaCl, and the mixture was partitioned between ether and water. The combined ether layers were dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by flash column chromatography on silica gel to produce 1.03 g (78.5% yield) of **33**: $[\alpha]^{25}_D$ −41.5° (*c* 0.4, CH_2Cl_2); IR (neat) 3060, 2950, 2920, 2880, 2850, 1660, 1650, 1630, 1530, 1340, 1150, 1110, 960, 890, 840 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.86 (s, 1 H), 8.79 (s, 1 H), 7.78 (d, J = 8.7 Hz, 1 H), 7.70 (d, J = 8.7 Hz, 1 H), 7.44 (d, J = 8.7 Hz, 1 H), 7.36 (dd, J = 8.7, 7.5 Hz, 1 H), 7.04 (d, J = 7.5 Hz, 1 H), 5.47 (s, 2 H), 5.34 (d, J = 6.0 Hz, 1 H), 5.31 (d, J = 6.0 Hz, 1 H), 5.30 (d, J = 3.6 Hz, 1 H), 4.29 (m, 1 H), 4.23 (m, 1 H), 3.74 (m, 1 H), 3.60 (s, 3 H), 3.58 (s, 3 H), 1.49 (d, J = 6.9 Hz, 3 H), 0.93 (s, 18 H), 0.16 (s, 3 H), 0.15 (s, 3 H), 0.14 (s, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 152.74, 148.97, 132.73, 132.18, 126.12, 125.58, 125.32, 124.20, 122.43, 122.24, 121.96, 120.57, 106.14, 103.43, 100.26, 94.78, 76.58, 75.80, 74.05, 69.27, 58.03, 56.37, 25.97, 25.90, 25.67, 18.10, 16.82, −3.95, −4.12, −4.22, −4.35 ppm; mass spectrum, *m/e* 654 (M^+), 622 (100%), 609, 591, 543; exact mass calcd for $C_{36}H_{54}O_7Si_2$ 654.3408, found 654.3429.

Dihydropyran Reduction, *C*-Glycosylanthracene 38. To a solution of **33** (1.96 g, 2.99 mmol) and a small amount of bromocresol green indicator in 20 mL of absolute ethanol were added $NaBH_3CN$ and methanolic HCl, prepared from 20 mL of acetyl chloride and 100 mL of methanol, alternately and gradually. The addition of hydride and acid was performed in such a way as to maintain the yellow color of the indicator (pH 4.5). The reaction was monitored by TLC and was complete within 3–4 h. The reaction was quenched with saturated aqueous $NaHCO_3$, and the mixture was extracted with hexane/ether (1/1). The combined organic phase was dried ($MgSO_4$) and evaporated. Flash column chromatography with hexane/CH_2Cl_2 (3/1) afforded 1.71 g of **38** (87% yield): $[\alpha]^{25}_D$ +22.6° (*c* 1.8, CH_2Cl_2); IR (neat) 3060, 2950, 2920, 2880, 2850, 1635, 1530, 1470, 1340, 1250, 1150, 1110, 1060, 960, 880, 830 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.82 (s, 1 H), 8.59 (s, 1 H), 7.88 (d, J = 8.7 Hz, 1 H), 7.67 (d, J = 8.7 Hz, 1 H), 7.59 (d, J = 8.7 Hz, 1 H), 7.37 (dd, J = 8.7, 7.5 Hz, 1 H), 7.04 (d, J = 7.5 Hz, 1 H), 5.47 (s, 2 H), 5.28 (d, J = 5.7 Hz, 1 H), 5.23 (d, J = 5.7 Hz, 1 H), 5.14 (dd, J = 11.4, 1.2 Hz, 1 H), 3.87 (ddd, J = 11.1, 8.1, 4.8 Hz, 1 H), 3.73 (s, 3 H), 3.59 (s, 3 H), 3.50 (dq, J = 9.0, 6.3 Hz, 1 H), 3.31 (dd, J = 9.0, 8.1 Hz, 1 H), 2.21 (ddd, J = 13.2, 4.5, 1.8 Hz, 1 H), 1.92–1.80 (m, 1 H), 1.33 (d, J = 6.3 Hz, 3 H), 0.94 (s, 9 H), 0.90 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 152.75, 149.61, 132.69, 132.24, 129.29, 127.17, 125.88, 125.46, 125.29, 123.79, 121.96, 121.13, 121.01, 105.94, 100.57, 94.73, 78.51, 77.37, 75.03, 71.78, 57.81, 56.33, 42.13, 29.67, 26.35, 26.18, 19.28, 18.31, 18.13, −2.58, −2.91, −3.76, −4.15 ppm; mass spectrum, *m/e* 656 (M^+), 480, 448, 423, 301, 147, 73 (100%); exact mass calcd for $C_{36}H_{56}O_7Si_2$ 656.3565, found 656.3544.

Stannane 39. To a solution of the reduced *C*-glycosylanthracene **38** (483 mg, 0.74 mmol) in 10 mL of THF was added 0.23 mL (1.52 mmol) of redistilled TMEDA. The solution was cooled to 0 °C, and 0.60 mL of *n*-butyllithium in hexanes (2.5 M, 1.50 mmol) was added over 10 min. The reaction mixture was stirred at 0 °C for 1 h and was cooled to −78 °C. To the cold dark green solution was added freshly distilled tributylchlorostannane dropwise until the green color of the anion was discharged (ca. 0.39 mL). The reaction mixture was stirred for 15 min at −78 °C and for 15 min at 0 °C. The reaction mixture was diluted with hexane/ether (1/1) and was washed with saturated aqueous NaCl. The organic extract was dried ($MgSO_4$) and evaporated. The residue was chromatographed on a short silica gel column, eluting with hexane/ether/triethylamine (5/1/0.005) to afford 643 mg of stannane **39** (92% yield): IR (neat) 3040, 2950, 2850, 1610, 1520, 1460, 1250, 1160, 1110, 950 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.74 (s, 1 H), 8.61 (s, 1 H), 7.86 (d, J = 9.0 Hz, 1 H), 7.79 (d, J = 8.1 Hz, 1 H), 7.57 (d, J = 8.7 Hz, 1 H), 7.45 (d, J = 8.4 Hz, 1 H), 5.28 (d, J = 5.7 Hz, 1 H), 5.22 (d, J = 5.7 Hz, 1 H), 5.18 (s, 2 H), 5.14 (dd, J = 11.7, 1.5 Hz, 1 H), 3.87 (ddd, J = 10.5, 8.1, 4.5 Hz, 1 H), 3.73 (s, 3 H), 3.67 (s, 3 H), 3.49 (dq, J = 9.0, 6.3 Hz, 1 H), 3.31 (dd, J = 9.0, 8.4 Hz, 1 H), 2.24–2.16 (ddd, J = 12.9, 4.5, 1.5 Hz, 1 H), 1.92–1.80 (m, 1 H), 1.61–1.53 (m, 6 H), 1.39–1.32 (m, 12 H), 1.21–1.15 (m, 6 H), 0.95 (s, 9 H), 0.92–0.87 (m, 9 H), 0.90 (s, 9 H), 0.17 (s, 3 H), 0.16 (s, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H) ppm.

Side Chain Introduction, Anthracene 40. To a solution of 126 mg (0.13 mmol) of stannane **39** under dry N_2 gas in 0.5 mL of anhydrous THF were sequentially added ca. 2 mg of $Pd_2(dba)_3CHCl_3$, ca. 2 mg of PPh_3, and a solution of 37 mg (0.13 mmol) of bromide **44** in 2.0 mL of THF. The reaction was conducted in a resealable sealed tube and was heated to 70 °C with stirring until the palladium catalyst precipitated from the solution (2–3 days) at which time TLC indicated that all starting material had been consumed. The solvent was evaporated from the reaction, and the residue was purified by flash column chromatography on silica gel with hexane/ether/triethylamine (4/1/0.005) as solvent. Anthracene **40** was isolated in 44% yield (47 mg) along with 12 mg of **38**, the product of protiodestannylation. Yields for this reaction varied up to 50% for **40**. Anthracene **40**: $[\alpha]^{23}_D$ −31.57° (c 0.0087, $CHCl_3$); IR (neat) 3060, 2930, 2890, 2860, 1745, 1630, 1540, 1470, 1390, 1360, 1250, 1220, 1160, 1110, 1080, 950, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.64 (s, 1 H), 8.58 (s, 1 H), 7.87 (d, J = 9.0 Hz, 1 H), 7.82 (d, J = 8.7 Hz, 1 H), 7.63 (d, J = 9.0 Hz, 1 H), 7.28 (d, J = 8.7 Hz, 1 H), 5.29–5.21 (m, 5 H), 5.15 (dd, J = 11.4, 1.2 Hz, 1 H), 5.06 (s, 1 H), 3.93 (s, 2 H), 3.87 (ddd, J = 10.8, 8.1, 4.8 Hz, 1 H), 3.73 (s, 3 H), 3.69 (s, 3 H), 3.49 (dq, J = 9.0, 6.3 Hz, 1 H), 3.31 (dd, J = 9.0, 8.4 Hz, 1 H), 2.20 (ddd, J = 13.2, 4.5, 1.5 Hz, 1 H), 1.90–1.78 (m, 1 H), 1.33 (d, J = 6.3 Hz, 3 H), 1.02 (s, 9 H), 0.94 (s, 9 H), 0.90 (s, 9 H), 0.16 (s, 3 H), 0.15 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 173.83, 163.03, 151.77, 149.65, 132.74, 132.48, 129.63, 127.27, 127.23, 127.09, 125.69, 125.63, 124.53, 122.08, 121.93, 121.31, 106.34, 100.64, 100.49, 96.17, 78.44, 77.39, 74.97, 71.72, 57.85, 57.70, 42.12, 34.34, 34.07, 29.66, 26.32, 26.17, 23.94, 19.25, 18.30, 18.11, −2.59, −2.93, −3.78, −4.18 ppm; mass spectrum, m/e (no M^+), 712, 650, 536, 479, 435, 417, 335, 301 (100%), 273, 231.

Dimethylcopperlithium Addition. Anthracene 41. To a suspension of 150 mg (0.80 mmol) of CuI in 2.0 mL of anhydrous ether at 0 °C was added 1.0 mL of an ether solution of methyllithium (1.4 M, 1.40 mmol) during 15 min. The solution was stirred for 15 min and then cooled to −78 °C, and a solution of 60 mg (0.073 mmol) of **40** in 2.0 mL of ether was added. The reaction mixture was stirred at −78 °C for 15 min and allowed to warm to −10 °C during a period of 2 h. TLC indicated that the reaction was complete. The reaction was quenched by the addition of 2.0 mL of a 1/1 (v/v) mixture of saturated aqueous ammonium hydroxide and ammonium chloride. The mixture was stirred in air at 0 °C for 30 min and extracted with ether. The ether phase was dried ($MgSO_4$), the solvent was evaporated, and the residue was purified by flash column chromatography on silica gel, eluting with hexane/ether/triethylamine (4/1/0.005) to produce 31 mg of **41** (51% yield) along with 15 mg (25% yield) of recovered starting material. Anthracene **41**: $[\alpha]^{23}_D$ −15.14° (c 0.0127, $CHCl_3$); IR (neat) 3060, 2960, 2940, 2900, 2860, 1760, 1640, 1540, 1470, 1400, 1390, 1360, 1350, 1300, 1250, 1160, 1110, 1060, 950, 900 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 8.61 (s, 1 H), 8.57 (s, 1 H), 7.85 (d, J = 9.0 Hz, 1 H), 7.75 (d, J = 8.7 Hz, 1 H), 7.60 (d, J = 9.0 Hz, 1 H), 7.42 (d, J = 8.7 Hz, 1 H), 5.27–5.21 (m, 4 H), 5.15 (dd, J = 11.4, 1.2 Hz, 1 H), 4.96 (s, 1 H), 3.87 (ddd, J = 11.1, 8.1, 4.8 Hz, 1 H), 3.73 (s, 3 H), 3.69 (s, 3 H), 3.49 (dq, J = 9.0, 6.3 Hz, 1 H), 3.31 (dd, J = 9.0, 8.4 Hz, 1 H), 3.26 (d, J = 13.8 Hz, 1 H), 3.15 (d, J = 13.8 Hz, 1 H), 2.90 (d, J = 16.5 Hz, 1 H), 2.53 (d, J = 16.5 Hz, 1 H), 2.22 (ddd, J = 13.2, 4.5, 1.5 Hz, 1 H), 1.90–1.78 (m, 1 H), 1.41 (s, 3 H), 1.36 (d, J = 6.3 Hz, 3 H), 1.00 (s, 9 H), 0.94 (s, 9 H), 0.89 (s, 9 H), 0.16 (s, 3 H), 0.15 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) 169.30, 152.00, 149.52, 132.55, 129.94, 129.39, 126.95, 125.69, 124.41, 124.17, 121.69, 121.31, 102.56, 100.56, 100.29, 78.45, 77.32, 76.15, 74.98, 71.77, 57.81, 57.76, 42.16, 41.98, 40.18, 34.75, 29.64, 26.31, 26.16, 24.81, 24.11, 19.24, 18.28, 18.10, −2.61, −2.94, −3.79, −4.19 ppm; mass spectrum, m/e 840 (M^+), 754, 710, 666, 477, 301, 231.

Oxidation to Anthraquinone 42. To a solution of 26 mg (0.031 mmol) of **41** in 5.0 mL of dry CH_2Cl_2 at 23 °C was added in small portions and with rapid stirring a mixture of bis(pyridine)silver permanganate and silica gel, prepared by stirring 77 mg (0.19 mmol) of the permanganate salt with 154 mg of silica gel 60 vigorously at 23 °C for 30 min. The oxidation was complete in 7 h. The reaction mixture was filtered, and the filter cake was washed thoroughly with CH_2Cl_2. The filtrate and combined washes was evaporated, and the residue was purified by column chromatography on silica gel, eluting with hexane/ether/triethylamine (1/1/0.005) to produce 23 mg (85% yield) of quinone **42**: $[\alpha]^{23}_D$ −80.99° (c 0.0117, $CHCl_3$); IR (neat) 2960, 2930, 2860, 1760, 1670, 1580, 1565, 1470, 1380, 1360, 1250, 1160, 1110 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 8.05 (d, J = 8.2 Hz, 1 H), 7.96 (d, J = 7.7 Hz, 1 H), 7.92 (d, J = 8.2 Hz, 1 H), 7.72 (d, J = 8.2 Hz, 1 H), 5.31 (d, J = 6.6 Hz, 1 H), 5.19 (d, J = 6.6 Hz, 1 H), 5.14 (d, J = 7.2 Hz, 1 H), 5.03 (d, J = 6.6 Hz, 1 H), 5.00 (dd, J = 11.8, 1.5 Hz, 1 H), 4.89 (s, 1 H), 3.80 (ddd, J = 11.0, 8.2, 4.8 Hz, 1 H), 3.62 (s, 3 H), 3.58 (s, 3 H), 3.42 (dq, J = 9.0, 6.1 Hz, 1 H), 3.21 (dd, J = 9.0, 8.4 Hz, 1 H), 3.20 (d, J = 13.8 Hz, 1 H), 3.08 (d, J = 13.8 Hz, 1 H), 2.81 (d, J = 16.4 Hz, 1 H), 2.53 (d, J = 16.4 Hz, 1 H), 2.33 (ddd, J = 13.3, 4.6, 2.0 Hz, 1 H), 1.47–1.38 (m, 1 H), 1.36 (s, 3 H), 1.31 (d, J = 6.0 Hz, 3 H), 0.95 (s, 9 H), 0.91 (s, 9 H), 0.85 (s, 9 H), 0.13 (s, 6 H), 0.11 (s, 3 H), 0.08 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 182.40, 182.26, 168.88, 156.67, 154.16, 143.41, 138.60, 137.17, 136.18, 135.84, 132.71, 124.35, 124.16, 124.00, 122.79, 102.39, 102.17, 78.32, 77.23, 75.55, 74.75, 71.72, 57.73, 57.64, 42.20, 41.54, 40.26, 34.77, 26.29, 26.14, 25.09, 24.11, 19.13, 18.24, 18.10, −2.64, −2.93, −3.78, −4.18 ppm; mass spectrum, m/e (no M^+), 839 ($M^+ - OCH_3$), 813 ($M^+ - t$-Bu), 769, 727, 683, 639, 595, 551, 519, 465, 433, 389, 345, 273, 143, 75 (100%); exact mass calcd for $C_{42}H_{61}O_{12}Si_2$ 813.3702, found 813.3743.

Vineomycinone B2 Methyl Ether (1). To a solution of 32 mg (0.037 mmol) of quinone **42** in 2.0 mL of methanol at 0 °C was added 5.0 mL of methanolic HCl, prepared from the addition of 0.3 mL of distilled acetyl chloride to 5.0 mL of methanol. The mixture was stirred at 0 °C for 30 min and at 25 °C for 4 h at which time TLC indicated a complete reaction. Solvent evaporation followed by column chromatography of the residue on silica gel eluting with $CHCl_3/CH_3OH$ (100/5) produced 14 mg (76% yield) of vineomycinone B2 methyl ester (**1**) as fine orange needles: mp 183–184 °C [lit.[7] mp 183–184 °C]; $[\alpha]^{23}_D$ +108.6° (c 0.000 68, $CDCl_3$); [lit.[7] $[\alpha]_D$ +109.1° (c 0.000 66, $CDCl_3$)]; IR (neat thin film deposited on NaCl from CH_2Cl_2) 3400 (br), 2930, 2860, 1735, 1630, 1440, 1375, 1260, 990, 970 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) 13.21 (s, 1 H), 13.09 (s, 1 H), 7.91 (d, J = 7.7 Hz, 1 H), 7.85 (d, J = 8.5 Hz, 1 H), 7.80 (d, J = 7.7 Hz, 1 H), 7.69 (d, J = 7.7 Hz, 1 H), 4.94 (dd, J = 10.5, 1.5 Hz, 1 H), 3.92 (s, 1 H), 3.86 (ddd, J = 11.1, 8.8, 5.0 Hz, 1 H), 3.72 (s, 3 H), 3.53 (dq, J = 9.2, 6.1 Hz, 1 H), 3.22 (dd, J = 9.2, 8.8 Hz, 1 H), 3.11 (d, J = 13.1 Hz, 1 H), 3.02 (d, J = 13.1 Hz, 1 H), 2.59 (d, J = 16.1 Hz, 1 H), 2.55 (d, J = 16.1 Hz, 1 H), 2.54 (ddd, J = 12.6, 4.6, 1.9 Hz, 1 H), 1.54–1.42 (m, 1 H), 1.42 (d, J = 6.1 Hz, 3 H), 1.30 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) 188.11, 173.27, 161.31, 158.92, 139.57, 138.24, 134.66, 133.29, 131.82, 131.75, 119.38, 118.88, 115.58, 115.43, 78.00, 75.90, 73.08, 71.82, 71.23, 51.74, 44.36, 40.46, 39.33, 27.25, 18.10 ppm; mass spectrum, m/e (no M^+), 384 (57), 281 (20), 280 (18), 207 (100), 117 (14), 111 (12), 109 (13), 99 (31), 97 (28); exact mass calcd for $C_{21}H_{20}O_7$ 384.1095, found 384.1152.

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Supplementary Material Available: Reproductions of ^1H and ^{13}C NMR, HMQC, and IR spectra for **1** (14 pages). Ordering information is given on any current masthead page.